Discovery of 'mixer cells' could improve healing

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French researchers from CNRS and Universite de Nice have recently identified cells that surprisingly change identity during embryogenesis in the Drosophila. By studying these "mixer cells" in a healing model, the scientists demonstrated that they helped to relax tissue tension, allowing perfect intercalation of the epidermis.

Published on 8 June in *PloS Biology*, these findings reveal how tissues adapt at the intercalation stage during embryonic development. They may also open a new path for research in regenerative medicine.

Multi-cellular organisms are made up of different cell types (skin, liver or neuronal cells, etc.). Deriving from non-specialized precursor cells, they become specialized as a result of a differentiation mechanism. In addition, during embryonic development, the cells are organized into separate, independent compartments that are essential to the correct assembly of organs. Within these compartments, the cells comply with two rules: once differentiated they retain their specific identity, and cells in a given compartment remain together, never mixing with those from another compartment. The scientists carried out their study on Drosophila embryos during "dorsal closure".

During this key stage of morphogenesis in the Drosophila, two epidermises meet and close together. This tissue intercalation is similar to the healing of a wound after a cut, and thus constitutes a good model for healing. By observing living embryos during the period of dorsal closure, the researchers observed one cell type that broke the two rules

mentioned above. Indeed, these "mixer cells" were able to change both identity and then compartment, under the normal conditions of embryonic development (e.g. without any lesion).

This shift of identity, or cell plasticity, was already known in a pathological setting (regeneration following a wound or disease, etc.) when, in most cases, the re-differentiation of a cell requires one or more cellular divisions. In this case, cell plasticity occurred without such an event.

The researchers demonstrated that it was controlled by specific genes that also intervene in tissue regeneration in the adult Drosophila: these genes constitute the JNK signaling pathway that also exists in vertebrates. This genetically-controlled cell plasticity mechanism is an unique type of cellular behavior that had never previously been observed during embryonic development.

Once differentiated, the mixer cells moved from one compartment to another, even though their boundaries were reputed to be impenetrable. Furthermore, tissue tension diminished as the number of cells that migrated to the destination compartment increased. The scientists discovered that by means of an as yet unknown process, the cell plasticity mechanism of mixer cells induced intercalation movements of nearby cells, thus endowing the tissues with an ability to adapt to the variations in tension that occur during embryonic morphogenesis.

To achieve this, a zone called "relaxation compartment" was created: this allowed tissues (in this case, the epidermis) to relax their tension during tissue intercalation. In this way, the intercalation of tissues during dorsal closure in the Drosophila embryo (a phenomenon similar to that of epidermal healing) could occur perfectly, i.e. without any visible scar.

This work has demonstrated a novel cell plasticity mechanism during

morphogenesis. In view of the similarities observed between the phenomenon of tissue intercalation studied here and skin healing, these results may provide a new path for the study of the cell mechanisms involved in the healing process.

More information: NK Signalling Controls Remodelling of the Segment Boundary through Cell Reprogramming during Drosophila Morphogenesis. Melanie Gettings, Fanny Serman, Raphaël Rousset, Patrizia Bagnerini, Luis Almeida, Stéphane Noselli. PloS Biology. 8 Juin 2010.

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